REMARKS

Status of the claims

Claims 57, 63, 64, 66, 68-71 and 87-102 are pending as shown in the paper filed August 22, 2006. Claims 91-102 (which were newly presented in the paper filed Aug. 22, 2006) have been entered but withdrawn from consideration as being directed to non-elected subject matter. (Office Action, paragraph 1).

By virtue of this response, claims 57 and 91 have been amended to recite an exogenous molecule. Support is found, for example, at page 3, lines 21-22 of the specification and in original claims 1 and 57. Claims 63, 68, 94 and 96 have been amended to correct antecedence in light of the amendments to claims 57 and 91.

Thus, claims 57, 63, 64, 66, 68-71 and 87-102 are pending and claims 57, 63, 64, 66, 68-71 and 87-90 are under consideration. Inasmuch as withdrawn claims 91-102 have been amended to contain all of the limitations of the elected composition claims, they are eligible for rejoinder upon allowance of the claims under consideration.

Objections and Rejections Withdrawn

The objection to the disclosure for containing an embedded hyperlink has been withdrawn in view of the previous amendments to the specification. (Office Action, paragraph 2). In addition, the objection to the specification for lack of compliance with the sequence rules has been withdrawn. (Office Action, paragraph 3). The objection to claim 68 has also been withdrawn. (Office Action, paragraph 4).

The rejection of claims 57, 63, 64, 66, 68, 70, 88 and 89 under 35 U.S.C. § 102(b) as allegedly anticipated by Crossley in light of Chen and Morceau has been withdrawn. (Office Action, paragraph 6). The rejection of claims 57, 66 and 71 under 35 U.S.C. § 103(a) as allegedly obvious over Crossley in view of Chen has also been withdrawn; as have the rejection of claims 57, 66 and 87 under 35 U.S.C. § 103(a) as allegedly obvious over Crossley in view of Chen and further in view of Hays, the rejection of claims 57, 66 and 90 under 35 U.S.C. § 103(a) based on Crossley in view of Chen and further in view of Gregory, and the rejection of claims 57, 66 and 69 under 35 U.S.C. § 103(a) based on

Crossley in view of Chen and further in view of Greisman. (Office Action, paragraphs 10, 11, 12 and 13).

35 U.S.C. § 101

Claims 57, 63, 64, 66, 68-71 and 87-90 were newly rejected under 35 U.S.C. § 101 as allegedly directed to non-statutory subject matter (Office Action, paragraph 5). In particular, it was alleged that these claims are somehow product-by-process claims and that the claimed products "do not sufficiently distinguish over chromatin complexes with protein as they exist naturally because the claims do not particularly point out any non-naturally occurring differences between the claimed products and the naturally occurring products." *Id.*

Claim 57 (from which all other claims directly or ultimately depend) recites (emphasis added):

> A complex between an **exogenous** molecule and a binding site in cellular chromatin, wherein the binding site comprises a target site and is in a region of cellular chromatin that is sensitive to a probe of chromatin structure.

This is not in any way a product-by-process claim. It is simply a product claim that contains entirely proper functional limitations. *See, e.g.,* M.P.E.P (Eighth Edition, revised August, 2006) § 2173.05(g): Functional Limitations.

Even assuming, for the sake of argument only, that the claims were somehow product-by-process claims, the resulting product is entirely distinguishable from naturally-occurring chromatin-protein complexes and from cells comprising these complexes. As noted above, the claims recite a complex between an exogenous molecule and a binding site in cellular chromatin. The specification defines "exogenous" as follows (page 11, lines 19-29 of the specification):

> An exogenous molecule is a molecule that is not normally present in a cell, but is introduced into a cell by one or more genetic, biochemical or other methods. An exogenous molecule can be, among other things, a small molecule, such as is generated by a combinatorial chemistry process, or a macromolecule such as a protein, nucleic acid, carbohydrate, lipid, glycoprotein or lipoprotien. For example, an exogenous nucleic acid can comprise

> an infecting viral genome, a plasmid or episome introduced into a cell, or a chromosome that is not normally present in the cell. Methods for the introduction of exogenous nucleic acids into cells are known to those of skill in the art and exemplary methods are described *infra*. An exogenous molecule can comprise, for example, a functioning version of a malfunctioning endogenous molecule or a malfunctioning version of a normally-functioning endogenous molecule.

Thus, the claimed complexes are clearly distinguishable from naturally occurring cellular chromatin-protein complexes because a naturally occurring chromatin-protein complex would never include an exogenous molecule as defined and claimed. The recitation "exogenous molecule" in all claims clearly indicates that the "hand of man" is present and, accordingly, the rejection should be withdrawn.

The Examiner also stated, without providing any supporting evidence, that "the breadth of the claimed subject matter includes products that have the same structure as naturally occurring protein-chromatin complexes." (Office Action at paragraph 5, page 3, *inter alia*). However, it should be clear that, as pointed out above, a complex of cellular chromatin with an exogenous molecule will have a different structure than a complex of cellular chromatin with an endogenous molecule, due to the structure of the exogenous molecule, which is not normally present in the cell.[1] For this reason, too, the rejection should be withdrawn.

35 U.S.C. §§ 102(b)/103(a)

A. Boyes

Claims 57, 63, 64 and 87-90 were newly rejected under 35 U.S.C. § 102(b) as allegedly anticipated by Boyes in light of Morceau and Hays and Gregory. (Office Action, paragraph 8). The Office Action states that Boyes shows that the binding of GATA-1 fragments to reconstituted chromatin results in disruption of the chromatin structure. *Id.* The Office then cites Morceau as allegedly demonstrating that GATA-1 is a zinc finger protein; Hays as showing that chromatin structure can be probed by

[1] This should be especially clear in the case of a complex containing an exogenous polypeptide (which will have a different amino acid sequence from any endogenous polypeptide) given the policy of the Office, with respect to biological molecules, to equate structure with sequence.

chemical probes; and Gregory for showing that chromatin structure can be probed by restriction endonucleases. *Id.*

Claims 57, 87 and 90 were also newly rejected under 35 U.S.C. § 103(a) as allegedly obvious over Boyes in view of Hays and Gregory. (Office Action, paragraph 16). Boyes, Hays and Gregory were cited as above and it was alleged that it would have been obvious to the skilled artisan to determine the chromatin structure of the complex of Boyes using the probes of Hays or Gregory and that, if such were done, it would establish that the complexes disclosed by Boyes are a species of the subject matter recited in claims 57, 87 and 90. *Id.*.

Applicants traverse the rejections. Boyes, alone or in light of Morceau, Hays and/or Gregory does not anticipate or render obvious the claimed complexes or cells comprising these complexes.

The pending claims relate to complexes between an exogenous molecule and a binding site in cellular chromatin, wherein the binding site lies in a region that is sensitive to a probe of chromatin structure, as well as cells comprising these complexes. According to the specification, "cellular chromatin" refers to endogenous chromatin, namely a genome as it is found naturally in a cell (see, page 10, lines 7-9 of the specification):

> Chromatin is the nucleoprotein structure comprising the cellular genome. Cellular chromatin comprises nucleic acid, primarily DNA, and protein, including histones and non-histone chromosomal proteins.

By contrast, and as acknowledged in the Office Action, all of the experiments described by Boyes are conducted *in vitro*, on reconstituted nucleosomes, not on cellular chromatin. See, for example, Boyes, page 530, first sentence of right column:

> To test the ability of GATA-1 to bind to its cognate site on a nucleosome, we reconstituted a 167 bp DNA fragment carrying six GATA-1 binding sites into a nucleosome by salt-urea dialysis.

In other words, Boyes in no way describes, demonstrates or suggests complexes as claimed comprising an exogenous polypeptide complexed to cellular chromatin. Rather, Boyes relates to an *in vitro*, extracellular complex between a protein and a DNA fragment that has been reconstituted into a nucleosome.

Morceau, in stating that GATA-1 contains cysteine-rich motifs that are reminiscent of a zinc finger structure (Morceau at page 542, first full paragraph), fails to add anything to supplement Boyes's lack of disclosure regarding exogenous polypeptides complexed to cellular chromatin. Likewise, the disclosure in Hays and Gregory of chemical or enzymatic probes cannot remedy the failings of Boyes.

Thus, the cited art does not show or in any way suggest the binding of an exogenous molecule to a site in cellular chromatin, let alone to a site in cellular chromatin that is sensitive to a probe of chromatin structure. Accordingly, the rejections should be withdrawn.

B. Stamatoyannopoulos

Claims 57, 63, 64, 66, 68, 70, 71 and 87-90 were newly rejected under 35 U.S.C. § 102(b) as allegedly anticipated by Stamatoyannopoulos in light of Morceau and Hays and Gregory. (Office Action, paragraph 9). Stamatoyannopoulos was cited for teaching analysis of a GATA-1 binding site in the human beta globin locus control region (LCR) as well as analysis of two types of cells: one (MEL) which is stably transformed with constructs of the LCR in which the GATA-1 binding site in the LCR is either mutated or normal, and is analyzed by use of DNase I; and another (Namalwa) comprising a human LCR region analyzed using micrococcal nuclease. *Id.* Morceau, Hays and Gregory were cited as above with regard to Boyes.

Claims 57, 87 and 90 were also newly rejected under 35 U.S.C. § 103(a) as allegedly obvious over Stamatoyannopoulos in view of Hays and Gregory. (Office Action, paragraph 17). Stamatoyannopoulos, Hays and Gregory were cited as above regarding the 102(b) rejection. *Id.* It was alleged that it would have been obvious to determine the chromatin structure of the complex of Stamatoyannopoulos by use of the probes of Hays and/or Gregory and that, if such were done, it would establish that the

GATA-1 complexes disclosed by Stamatoyannopoulos are a species of the subject matter recited in claims 57, 87 and 90. *Id.*

To reiterate, the pending claims are drawn to complexes comprising cellular chromatin and an exogenous molecule. With respect to the experiments involving MEL cells disclosed by Stamatoyannopoulos, Applicants note that GATA-1 is endogenous to MEL cells. *See*, for example, Stamatoyannopoulos at page 108, first column: "An important property of these [MEL] cells is that they preferentially express GATA-1 . . ." and Stamatoyannopoulos at page 113, first column, first (incomplete) paragraph: "Because MEL cells almost exclusively express GATA-1 [*citation omitted*], our results imply that this particular GATA binding factor is functional in HS formation." Thus, this reference fails to show a complex in MEL cells comprising an exogenous molecule, as claimed.

With respect to the second cell type disclosed by Stamatoyannopoulos, (*i.e.*, Namalwa cells), Applicants note that Figure 6 of Stamatoyannopoulos (cited in the Office Action at paragraph 9, page 6) discloses the results of an experiment in which isolated nuclei from Namalwa cells were treated with micrococcal nuclease.[2] Such does not describe a complex between an exogenous molecule and cellular chromatin, but rather cleavage of chromatin between nucleosomes. *See*, for example, Stamatoyannopoulos at page 110, second column: "MNase preferentially cuts between nucleosomes and therefore allows their position to be determined by Southern blot analysis."

In sum, Stamatoyannopoulos, either alone or in combination with the secondary references, fails to disclose or suggest a complex, as claimed, in which an exogenous molecule is present in a region of cellular chromatin that is sensitive to a probe of chromatin structure. Accordingly, the rejections should be withdrawn.

[2] Stamatoyannopoulos also describes experiments in which naked DNA fragments were incubated with nuclear extracts from Namalwa cells (page 109, second column, first full paragraph; results shown in Figure 4 on page 110). These experiments also fail to disclose or suggest a complex between an exogenous molecule and cellular chromatin.

35 U.S.C. § 103(a): Stamatoyannopoulos in view of Greisman[3]

Claims 57, 66 and 69 were newly rejected as allegedly obvious over Stamatoyannopoulos in view of Greisman (Office Action, paragraph 18). Stamatoyannopoulos was cited as above, but was acknowledged not to show plant cells comprising exogenous polypeptides bound to chromatin. *Id.* Gresiman is cited as disclosing methods for selecting high-affinity zinc finger proteins for diverse DNA target sites and stating that such proteins provide means for developing plants with altered phenotypes. *Id.*

Applicants respectfully traverse the rejection and supporting remarks. As set forth above, Stamatoyannopoulos fails to disclose or suggest the claimed complexes. Greisman, for its part, fails to remedy the deficiencies of the primary reference. Moreover, the Examiner has not provided evidence for any motivation in the art, as of the filing date, to combine these references; relying instead on a general assertion that such a combination would allow one of skill in the art to pursue further research.

Accordingly, withdrawal of the rejection is requested.

[3] Applicants assume that U.S Patent No. 6,410,248 is the intended reference. Clarification is requested.

CONCLUSION

For the reasons set forth herein, Applicants believe that the claims under consideration recite statutory subject matter, are novel and are non-obvious. Accordingly, allowance of the claims under consideration, and rejoinder and allowance of the withdrawn claims, are requested.

Respectfully submitted,

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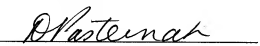
By: 

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